REMARKS

Favorable reconsideration of the subject application is respectfully requested in view of the following remarks. Claims 23, 24, 29-36 and 41-46 are currently under consideration in this application. Applicants acknowledge the allowability of claims 23, 24 and 35 and 36, drawn to methods for detecting prostate cancer employing primers specific for a polynucleotide sequence of SEQ ID NO: 110.

Claims 29-34 and 41-46, however, remain rejected under 35 U.S.C. § 101, as allegedly lacking specific utility. The Examiner asserts that a skilled artisan would not reasonably expect that a prostate specific sequence, such as those claimed, would have utility in methods for the detection of prostate cancer in a patient, absent an experimental showing that cells expressing such sequences are in fact detected in a patient sample, *e.g.*, a blood sample. Applicants traverse this rejection, for reasons already of record in these proceedings, and further in view of the comments below.

According to the Examiner, only claims having the subject matter of SEQ ID NO: 110 satisfy the utility requirements of 35 U.S.C. § 101, apparently in view of the previously submitted Declaration of Raymond Houghton, Ph.D., demonstrating the detection of SEQ ID NO: 110 in peripheral blood samples from prostate cancer patients. However, the Examiner maintains that, "SEQ ID NO: 110 is different from the claimed sequences of SEQ ID NO: 172-175, 177, 223 and 224 in that only SEQ ID No: 110 has been detected as having a high level of expression in serum of patients with prostate cancer, as compared to normal healthy human..." (page 3; Office Action dated February 27, 2002). Thus the Examiner is apparently of the belief that absent a specific experimental showing that SEQ ID NOs: 172-175, 177, 223 and 224 are also detectable in, for example, blood samples from prostate cancer patients, the claimed invention drawn to these SEQ ID NOs: lacks patentable utility under 35 U.S.C. § 101.

Applicants respectfully traverse this rejection on the basis that it is not necessary, in order to satisfy the utility requirements of 35 U.S.C. § 101, to demonstrate experimentally that SEQ ID NOs: 172-175, 177, 223 and 224 can be detected in blood samples from prostate cancer patients, when the skilled artisan, in view of Applicants' disclosure, and in view of the general level of knowledge in this art, would fully recognize a reasonable likelihood of success in practicing such methods.

In this respect, it is submitted that the Examiner has applied against Applicants a standard for patentable utility that exceeds the requirements proscribed by 35 U.S.C. § 101. An applicant is not required to provide evidence sufficient to establish that an asserted utility is true "beyond a reasonable doubt." *In re Irons*, 340 F.2d 974, 978, 144 USPQ 351, 354 (CCPA 1965; emphasis added); *See also* MPEP 2107.02. Moreover, an applicant need not provide evidence that establishes an asserted utility "as a matter of statistical certainty." Rather, a rigorous correlation is not necessary when a test is reasonably predictive of a result. *Nelson v. Bowler*, 626 F.2d 853, 856-57, 206 USPQ 881, 883-84 (CCPA 1980; emphasis added). Further still, in order to overcome the presumption of truth that an assertion of utility by the Applicant enjoys, Office personnel must establish that it is more likely than not that one of ordinary skill in the art would doubt (*i.e.*, "question") the truth of the statement of utility." (*e.g.*, MPEP 2107.02 IIIA; emphasis added).

Applicants maintain that the skilled artisan would more likely than not concur that the Applicants' claimed sequences, based upon their identified prostate-specific expression profiles, indeed possess utility under 35 U.S.C. § 101 in the context of the claimed invention, irrespective of whether Applicants have presented experimental confirmation for each and every sequence currently claimed.

The Examiner cites Gelmini *et al.*, 2001, Clin Chem Lab Med, 39(5): 385-91, as allegedly supporting the position that the skilled artisan, "would not have expected that the presence of prostate cells in circulation would be useful for distinguishing between localized and advanced or metastasized prostate carcinoma." Applicants note, however, that utility under 35 U.S.C. § 101 is to be evaluated on the basis of the claimed invention. The claims currently under consideration are drawn to methods for detecting prostate cancer in a patient. The currently claimed invention is not drawn to methods for "distinguishing between localized and advanced or metastasized prostate carcinoma." Moreover, Applicants have not attempted to establish that the SEQ ID NOs: of the instant claims have utility in distinguishing between localized and advanced or metastasized prostate cancer, although there would be an expectation that they would in view of the instant disclosure. What Applicants have asserted as the basis for one illustrative utility is that prostate-specific sequences such as those claimed are useful in the detection of prostate cancer employing art-recognized techniques. As prostate-specific markers are not detectable in the serum of normal individuals, the identification of the presence of a

prostate-specific marker in the circulation of a patient is indicative of the presence of prostate cancer in the patient, and would be recognized as such by the skilled individual in the art. Moreover, this utility for detecting the presence of prostate cancer in a patient would be recognized by the skilled artisan irrespective of whether the claimed sequences were also demonstrated "useful for distinguishing between localized and advanced or metastasized prostate carcinoma."

Applicants further submit that the disclosure of Gelmini *et al.* is indeed entirely consistent with Applicants' position that prostate-specific sequences are useful in the detection of prostate cancer. Gelmini *et al.* discloses, for example, that the, "specific detection of prostate-derived cells in peripheral blood seems to be a promising tool." (Gelmini *et al.*, page 385) Gelmini *et al.* further describes, using a new polymerase chain reaction developed in conjunction with this promising tool, that 32% of peripheral blood samples from prostate cancer patients were positive by this approach, whereas no positive samples were found in the control group of healthy subjects. (*e.g.*, Abstract; see also page 388) Thus, Gelmini *et al.* fully supports the position that a prostate-specific sequence can be used for detecting prostate cancer in a patient, which is the position Applicants have maintained during these proceedings, and which is the subject matter of Applicants' claimed invention.

The Examiner also cites Kibel et al and Ren *et al.* as allegedly teaching the skilled artisan that "it is unpredictable that metastasized prostate cells still express the claimed sequences because expression of a sequence could be lost during the progression toward metastasis." The Examiner concludes that "one would not have expected that the claimed sequences are useful for diagnostic and prognostic information about the presence in a subject of an invasive prostate tumor.

However, again, if the proper legal standard sufficient for establishing utility under 35 U.S.C. § 101 is applied against the instant claims, the disclosures of Gelmini *et al.*, Kibel *et al.* and Ren *et al.*, taken either individually, or in combination, do not negate the skilled artisan's recognition that Applicants' asserted utilities are more likely than not true. Applicants certainly acknowledge that, in some instances, a protein may have altered expression in metastatic cancer versus primary cancer, as suggested by the Examiner. This does not, however, compromise the general contention set forth by

Applicants that there would be a reasonable expectation that the prostate-specific sequences currently claimed are useful in the detection of prostate cancer in a patient.

Therefore, collectively, in view of Applicants' specification as originally filed, in view of the previously submitted Declaration of Raymond Houghton, Ph.D., and further in view of the level of general knowledge in this art, Applicants submit that the skilled artisan would expect that the presently claimed invention possesses patentable utility under 35 U.S.C. § 101. Applicants thus respectfully request that the Examiner's rejections under 35 U.S.C. § 101, and the related rejection under 35 U.S.C. § 112, first paragraph, be reconsidered and withdrawn.

All of the claims remaining in this application are believed to be in condition for allowance. The Examiner is invited to contact the undersigned at (206) 622-4900 with any questions, comments and/or suggestions pertaining to this matter.

Respectfully submitted,

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